

CLAIMS

What is claimed is:

1. An isolated fragment of SEQ ID NO:10, having the ability to inhibit tumor growth.
- 5 2. The isolated fragment of Claim 1, wherein the fragment is SEQ ID NO:37.
3. The isolated fragment of Claim 1, wherein the fragment is reduced.
4. The isolated fragment of Claim 1, wherein the fragment is alkylated.
5. The isolated fragment of Claim 1, wherein the fragment is oxidized.
- 10 6. An isolated mutated fragment of SEQ ID NO:10, wherein one or more, and five or fewer, amino acids have been substituted, and wherein the mutated fragment has the ability to inhibit tumor growth.
7. The isolated mutated fragment of Claim 6, wherein the fragment is reduced.
8. The isolated mutated fragment of Claim 6, wherein the fragment is alkylated.
9. The isolated mutated fragment of Claim 6, wherein the fragment is oxidized.
- 15 10. The isolated fragment of Claim 6, wherein the fragment is SEQ ID NO:38.
11. The isolated fragment of Claim 6, wherein the fragment is SEQ ID NO:39.

12. The isolated fragment of Claim 6, wherein the fragment is SEQ ID NO:40.
13. The isolated fragment of Claim 6, wherein the fragment is SEQ ID NO:41.
14. The isolated fragment of Claim 6, wherein the fragment is SEQ ID NO:42.
15. An isolated fragment of SEQ ID NO:10, having the ability to inhibit
5 angiogenesis.
16. The isolated fragment of Claim 15, wherein the fragment is SEQ ID NO:37.
17. The isolated fragment of Claim 15, wherein the fragment is reduced.
18. The isolated fragment of Claim 15, wherein the fragment is alkylated.
19. The isolated fragment of Claim 15, wherein the fragment is oxidized.
- 10 20. An isolated mutated fragment of SEQ ID NO:10, wherein one or more, and five
or fewer, amino acids have been substituted, and wherein the mutated fragment
has the ability to inhibit angiogenic activity.
21. The isolated mutated fragment of Claim 20, wherein the fragment is reduced.
22. The isolated mutated fragment of Claim 20, wherein the fragment is alkylated.
- 15 23. The isolated mutated fragment of Claim 20, wherein the fragment is oxidized.
24. The isolated fragment of Claim 20, wherein the fragment is SEQ ID NO:38.

25. The isolated fragment of Claim 20, wherein the fragment is SEQ ID NO:39.
26. The isolated fragment of Claim 20, wherein the fragment is SEQ ID NO:40.
27. The isolated fragment of Claim 20, wherein the fragment is SEQ ID NO:41.
28. The isolated fragment of Claim 20, wherein the fragment is SEQ ID NO:42.
- 5 29. An isolated fragment of SEQ ID NO:10, having the ability to inhibit protein synthesis in endothelial cells.
30. The isolated fragment of Claim 29, wherein the fragment is SEQ ID NO:37.
31. The isolated fragment of Claim 29, wherein the fragment is reduced.
32. The isolated fragment of Claim 29, wherein the fragment is alkylated.
- 10 33. The isolated fragment of Claim 29, wherein the fragment is oxidized.
34. An isolated mutated fragment of SEQ ID NO:10, wherein one or more, and five or fewer, amino acids have been substituted, and wherein the mutated fragment has the ability to inhibit protein synthesis in endothelial cells.
35. The isolated mutated fragment of Claim 34, wherein the fragment is reduced.
- 15 36. The isolated mutated fragment of Claim 34, wherein the fragment is alkylated.
37. The isolated mutated fragment of Claim 34, wherein the fragment is oxidized.

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- The isolated fragment of Claim 34, wherein the fragment is SEQ ID NO:38.
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- The isolated fragment of Claim 34, wherein the fragment is SEQ ID NO:39.
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- The isolated fragment of Claim 34, wherein the fragment is SEQ ID NO:40.
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- The isolated fragment of Claim 34, wherein the fragment is SEQ ID NO:41.
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42.
- The isolated fragment of Claim 34, wherein the fragment is SEQ ID NO:42.
43.
- A method for inhibiting tumor growth in mammalian tissue, the method comprising contacting the tissue with a composition comprising an isolated fragment selected from the group consisting of:
- (a)
- SEQ ID NO:10;
- 10
- (b)
- amino acid 2 through amino acid 245 of SEQ ID NO:10;
- (c)
- SEQ ID NO:19;
- (d)
- amino acid 1 through amino acid 125 of SEQ ID NO:10;
- (e)
- SEQ ID NO:20;
- (f)
- SEQ ID NO:21;
- 15
- (g)
- SEQ ID NO:22;
- (h)
- SEQ ID NO:23;
- (i)
- SEQ ID NO:25;
- (j)
- SEQ ID NO:26;
- (k)
- SEQ ID NO:29;
- 20
- (l)
- SEQ ID NO:30;
- (m)
- SEQ ID NO:33;
- (n)
- SEQ ID NO:34;
- (o)
- SEQ ID NO:37;
- (p)
- SEQ ID NO:38;

- (q) SEQ ID NO:39;
- (r) SEQ ID NO:40;
- (s) SEQ ID NO:41; and
- (t) SEQ ID NO:42.

5 44. The method of Claim 43, wherein the fragment is reduced.

45. The method of Claim 43, wherein the fragment is alkylated.

46. The method of Claim 43, wherein the fragment is oxidized.

47. The method of Claim 43, wherein one or more of the cysteine residues have been substituted for another amino acid.

10 48. A method for inhibiting angiogenic activity in mammalian tissue, the method comprising contacting the tissue with a composition comprising an isolated fragment selected from the group consisting of:

- (a) SEQ ID NO:10;
- (b) amino acid 2 through amino acid 245 of SEQ ID NO:10;
- 15 (c) SEQ ID NO:19;
- (d) amino acid 1 through amino acid 125 of SEQ ID NO:10;
- (e) SEQ ID NO:20;
- (f) SEQ ID NO:21;
- (g) SEQ ID NO:22;
- 20 (h) SEQ ID NO:23;
- (i) SEQ ID NO:25;
- (j) SEQ ID NO:26;
- (k) SEQ ID NO:29;
- (l) SEQ ID NO:30;

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- (m)

SEQ ID NO:33;
- (n)

SEQ ID NO:34;
- (o)

SEQ ID NO:37;
- (p)

SEQ ID NO:38;
- (q)

SEQ ID NO:39;
- (r)

SEQ ID NO:40;
- (s)

SEQ ID NO:41; and
- (t)

SEQ ID NO:42.
49.
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A method for inhibiting protein synthesis in one or more mammalian cells, the method comprising contacting the one or more cells with a composition comprising an isolated fragment selected from the group consisting of:
- (a)

SEQ ID NO:10;
- (b)

amino acid 2 through amino acid 245 of SEQ ID NO:10;
- (c)

SEQ ID NO:19;
- 15

(d) amino acid 1 through amino acid 125 of SEQ ID NO:10;
- (e)

SEQ ID NO:20;
- (f)

SEQ ID NO:21;
- (g)

SEQ ID NO:22;
- (h)

SEQ ID NO:23;
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(i) SEQ ID NO:25;
- (j)

SEQ ID NO:26;
- (k)

SEQ ID NO:29;
- (l)

SEQ ID NO:30;
- (m)

SEQ ID NO:33;
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(n) SEQ ID NO:34;
- (o)

SEQ ID NO:37;
- (p)

SEQ ID NO:38;
- (q)

SEQ ID NO:39;

- (r) SEQ ID NO:40;
- (s) SEQ ID NO:41; and
- (t) SEQ ID NO:42.

50. A method for inhibiting protein synthesis in one or more mammalian cells, the
5 method comprising contacting the one or more cells with a composition
comprising an isolated fragment selected from the group consisting of:
- (a) SEQ ID NO:2;
 - (b) SEQ ID NO:6; and
 - (c) SEQ ID NO:10.
- 10 51. The isolated fragment of Claim 29, wherein the protein synthesis is cap-
dependent protein synthesis.
52. The method of Claim 49, wherein the protein synthesis is cap-dependent protein
synthesis.
53. The method of Claim 50, wherein the protein synthesis is cap-dependent protein
15 synthesis.
54. The isolated fragment of Claim 29, wherein the endothelial cells express the
 $\alpha_v\beta_3$ integrin.
55. The method of Claim 49, wherein the mammalian cells express the $\alpha_v\beta_3$
integrin.
- 20 56. The method of Claim 50, wherein the mammalian cells express the $\alpha_v\beta_3$
integrin.

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57. An isolated peptide of the formula:



- 5 wherein R^1 is hydrogen or a peptidyl chain of 1 to 17 amino acids, R^2 is hydrogen or a peptidyl chain of 1 to 12 amino acids, and X^1 , X^2 and X^3 are individually an amino acid, and wherein said peptide inhibits tumor growth.

58. The isolated peptide of Claim 57, wherein X^1 is an amino acid with a basic side chain or an amino acid with an aromatic side chain.

59. The isolated peptide of Claim 58, wherein X^1 is phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, glutamine or asparagine.

- 10 60. The isolated peptide of Claim 59, wherein X^1 is lysine or phenylalanine.

61. The isolated peptide of Claim 57, wherein X^2 , X^3 and X^4 are independently an amino acid with a hydrophilic side chain or an amino acid with a basic side chain.

- 15 62. The isolated peptide of Claim 61, wherein X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.

63. The isolated peptide of Claim 62, wherein X^2 and X^4 are independently cysteine, serine or aspartic acid and X^3 is cysteine or aspartic acid.

- 20 64. The isolated peptide of Claim 57, wherein X^1 is phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, glutamine or asparagine and X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.

65. The isolated peptide of Claim 57, wherein R^1 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, or 8 amino acid residues.
66. The isolated peptide of Claim 65, wherein said amino acid or peptidyl chain represented by R^1 is selected from the group consisting of:
- 5 (a) P;
 - (b) MP;
 - (c) TMP;
 - (d) TTMP (SEQ ID NO:46);
 - (e) FTTMP (SEQ ID NO:47);
 - 10 (f) RFTTMP (SEQ ID NO:48);
 - (g) QRFTTMP (SEQ ID NO:49);
 - (h) LQRFTTMP (SEQ ID NO:50);
 - (i) KQRFTTMP (SEQ ID NO:51); and
 - (j) a conservative variant of any of (a)-(i).
- 15 67. The isolated peptide of Claim 57, wherein R^2 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, 8 or 9 amino acid residues.
68. The isolated peptide of Claim 67, wherein said amino acid or peptidyl chain represented by R^2 is selected from the group consisting of:
- (a) A;
 - 20 (b) AS;
 - (c) ASR;
 - (d) ASRN (SEQ ID NO:52);
 - (e) ASRND (SEQ ID NO:53);
 - (f) ASRNDY (SEQ ID NO:54);
 - 25 (g) ASRNDYS (SEQ ID NO:55);
 - (h) ASRNDYSY (SEQ ID NO:56);

- (i) ASRNDYSYW (SEQ ID NO:57);
- (j) ASRNDYSYWL (SEQ ID NO:58); and
- (k) a conservative variant of any of (a)-(j).

69. The isolated peptide of Claim 57, wherein the peptide is reduced.
- 5 70. The isolated peptide of Claim 57, wherein the peptide is alkylated.
71. The isolated peptide of Claim 57, wherein the peptide is oxidized.
72. An isolated peptide of the formula:

$$R^1X^1LFX^2NVNX^3VX^4NFR^2$$
 (SEQ ID NO:45),
 wherein R^1 is hydrogen or a peptidyl chain of 1 to 17 amino acids, R^2 is
 10 hydrogen or a peptidyl chain of 1 to 12 amino acids, and X^1 , X^2 and X^3 are
 individually an amino acid, and wherein said peptide inhibits angiogenic activity
 in mammalian tissue.
73. The isolated peptide of Claim 72, wherein X^1 is an amino acid with a basic side
 chain or an amino acid with an aromatic side chain.
- 15 74. The isolated peptide of Claim 73, wherein X^1 is phenylalanine, tyrosine,
 tryptophan, lysine, arginine, histidine, glutamine or asparagine.
75. The isolated peptide of Claim 74, wherein X^1 is lysine or phenylalanine.
76. The isolated peptide of Claim 72, wherein X^2 , X^3 and X^4 are independently an
 amino acid with a hydrophilic side chain or an amino acid with a basic side
 20 chain.

11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

77. The isolated peptide of Claim 76, wherein X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.
78. The isolated peptide of Claim 77, wherein X^2 and X^4 are independently cysteine, serine or aspartic acid and X^3 is cysteine or aspartic acid.
- 5 79. The isolated peptide of Claim 72, wherein X^1 is phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, glutamine or asparagine and X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.
80. The isolated peptide of Claim 72, wherein R^1 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, or 8 amino acid residues.
- 10 81. The isolated peptide of Claim 80, wherein said amino acid or peptidyl chain represented by R^1 is selected from the group consisting of:
- (a) P;
 - (b) MP;
 - (c) TMP;
 - 15 (d) TTMP (SEQ ID NO:46);
 - (e) FTTMP (SEQ ID NO:47);
 - (f) RFTTMP (SEQ ID NO:48);
 - (g) QRFTTMP (SEQ ID NO:49);
 - (h) LQRFTTMP (SEQ ID NO:50);
 - 20 (i) KQRFTTMP (SEQ ID NO:51); and
 - (j) a conservative variant of any of (a)-(i).
82. The isolated peptide of Claim 72, wherein R^2 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, 8 or 9 amino acid residues.

83. The isolated peptide of Claim 82, wherein said amino acid or peptidyl chain represented by R^2 is selected from the group consisting of:
- (a) A;
 - (b) AS;
 - 5 (c) ASR;
 - (d) ASRN (SEQ ID NO:52);
 - (e) ASRND (SEQ ID NO:53);
 - (f) ASRNDY (SEQ ID NO:54);
 - (g) ASRNDYS (SEQ ID NO:55);
 - 10 (h) ASRNDYSY (SEQ ID NO:56);
 - (i) ASRNDYSYW (SEQ ID NO:57);
 - (j) ASRNDYSYWL (SEQ ID NO:58); and
 - (k) a conservative variant of any of (a)-(j).
84. The isolated peptide of Claim 72, wherein the peptide is reduced.
- 15 85. The isolated peptide of Claim 72, wherein the peptide is alkylated.
86. The isolated peptide of Claim 72, wherein the peptide is oxidized.
87. An isolated peptide of the formula:
- $$R^1X^1LFX^2NVNX^3VX^4NFR^2 \text{ (SEQ ID NO:45),}$$
- wherein R^1 is hydrogen or a peptidyl chain of 1 to 17 amino acids, R^2 is
- 20 hydrogen or a peptidyl chain of 1 to 12 amino acids, and X^1 , X^2 and X^3 are individually an amino acid, and wherein said peptide inhibits protein synthesis in endothelial cells.
88. The isolated peptide of Claim 87, wherein X^1 is an amino acid with a basic side chain or an amino acid with an aromatic side chain.

89. The isolated peptide of Claim 88, wherein X^1 is phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, glutamine or asparagine.
90. The isolated peptide of Claim 89, wherein X^1 is lysine or phenylalanine.
- 5 91. The isolated peptide of Claim 87, wherein X^2 , X^3 and X^4 are independently an amino acid with a hydrophilic side chain or an amino acid with a basic side chain.
92. The isolated peptide of Claim 91, wherein X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.
- 10 93. The isolated peptide of Claim 92, wherein X^2 and X^4 are independently cysteine, serine or aspartic acid and X^3 is cysteine or aspartic acid.
94. The isolated peptide of Claim 87, wherein X^1 is phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, glutamine or asparagine and X^2 , X^3 and X^4 are independently cysteine, serine, threonine, aspartic acid or glutamine.
- 15 95. The isolated peptide of Claim 87, wherein R^1 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, or 8 amino acid residues.
96. The isolated peptide of Claim 95, wherein said amino acid or peptidyl chain represented by R^1 is selected from the group consisting of:
- 20 (a) P;
 (b) MP;
 (c) TMP;
 (d) TTMP (SEQ ID NO:46);
 (e) FTTMP (SEQ ID NO:47);

- (f) RFTTMP (SEQ ID NO:48);
 (g) QRFTTMP (SEQ ID NO:49);
 (h) LQRFTTMP (SEQ ID NO:50);
 (i) KQRFTTMP (SEQ ID NO:51); and
 5 (j) a conservative variant of any of (a)-(i).

97. The isolated peptide of Claim 87, wherein R^2 is one amino acid or a peptidyl chain of 2, 3, 4, 5, 6, 7, 8 or 9 amino acid residues.

98. The isolated peptide of Claim 97, wherein said amino acid or peptidyl chain represented by R^2 is selected from the group consisting of:

- 10 (a) A;
 (b) AS;
 (c) ASR;
 (d) ASRN (SEQ ID NO:52);
 (e) ASRND (SEQ ID NO:53);
 15 (f) ASRNDY (SEQ ID NO:54);
 (g) ASRNDYS (SEQ ID NO:55);
 (h) ASRNDYSY (SEQ ID NO:56);
 (i) ASRNDYSYW (SEQ ID NO:57);
 (j) ASRNDYSYWL (SEQ ID NO:58); and
 20 (k) a conservative variant of any of (a)-(j).

99. The isolated peptide of Claim 87, wherein the peptide is reduced.

100. The isolated peptide of Claim 87, wherein the peptide is alkylated.

101. The isolated peptide of Claim 87, wherein the peptide is oxidized.

102. A method for inhibiting tumor growth in mammalian tissue, the method comprising contacting the tissue with a composition comprising the isolated peptide of Claim 57.
- 5 103. A method for inhibiting angiogenic activity in mammalian tissue, the method comprising contacting the tissue with a composition comprising the isolated peptide of Claim 72.
104. A method for inhibiting protein synthesis in one or more mammalian cells, the method comprising contacting the one or more cells with a composition comprising the isolated peptide of Claim 87.
- 10 105. The isolated peptide of Claim 57, combined with a pharmaceutically-acceptable carrier.
106. The isolated peptide of Claim 72, combined with a pharmaceutically-acceptable carrier.
- 15 107. The isolated peptide of Claim 87, combined with a pharmaceutically-acceptable carrier.